

Application No. 10/021,602  
Amendment dated January 24, 2005  
Reply to Office Action of December 1, 2004

**Remarks**

Applicants have cancelled claim 43 and amended claims 5 and 44. Claims 5 and 44-57 remain in the application. Applicants respectfully request reconsideration of the amended claims.

Applicants appreciate the opportunity to interview the Examiner on January 21, 2005 during which the amended claims and cited references were discussed. The Examiner objected to the word "about" in amended claim 5, and Applicants have changed claim 5 to the more limiting "substantially." In addition, portions of the Remarks were also discussed. It is Applicants understanding that the Examiner will withdraw the rejection of the claims based on Fisch and Tolles, but a final disposition of the claims is subject to the results of a followup search.

Claims 5 and 43-57 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. RE 35,589 to Fisch in view of U.S. Patent No. 4,171,866 to Tolles. Fisch relates to a hemocytometer that is simple to use, inexpensive to make and disposable after use. The hemocytometer facilitates the counting of cells in a liquid sample under magnification using a grid etched into slide covers. In Fig. 1, Fisch shows a slide 2 and slide covers 3, 3' separated by a film 23 and a separating wall 26. In Figs. 3a and 3b, a slide cover 40 has thin film spacers 49 located at the corners of the slide cover. In Fig. 3c, the slide cover 40 has a film pattern 46' that can act as a spacer, and its diameter can be increased to eliminate the spacers 49. The device in Fisch is designed expressly so that a liquid sample can be observed under a microscope through the slide cover.

Tolles relates to a hemocytometer, and the Office Action refers to the prior art device of Figs. 1 and 2, which has a glass base plate 11 with upwardly extending integral lands 12. A depth chamber 14 is formed with a counting grid 15 inscribed in the bottom of the chamber 14. A cover glass 13 is placed over the lands 12, and a number of blood cells is counted within the grid area 15.

In order to establish a *prima facie* case of obviousness, it is necessary that the Office Action present evidence, preferably in the form of some teaching, suggestions, incentives or inference in the applied prior art or, in the form of generally available

Application No. 10/021,602  
Amendment dated January 24, 2005  
Reply to Office Action of December 1, 2004

knowledge, that one having ordinary skill in the art would have been led to arrive at the claimed invention.

Applicants submit that a *prima facie* case of obviousness is not made because the cited references in combination do not teach, suggest or motivate one to provide a hybridization apparatus having the elements recited in amended claim 5.

First, claim 5 requires a cover slip having a thickness of substantially 1 mm, which is a thickness sufficient to provide a cover slip beam stiffness that prevents adhesion forces created by the introduction of hybridization liquid into the hybridization chamber from substantially changing a substantially constant distance between the bottom surface of the cover slip and the top surface of the substrate.

In Fisch, the covering substrate 30 is transparent glass in the range of 0.1 to 0.5 mm thick with an exemplary thickness of 0.33 mm as described with respect to Fig. 4. The purpose of Fisch is to provide a small chamber in which cells can be microscopically counted. The Office Action in paragraph 2 of page 2 concludes that the Fisch cover glass thickness "would provide sufficient beam stiffness and allow reaction of the adhesion forces." However, claim 5 requires the cover slip beam thickness prevent adhesion forces from changing the distance between the cover slip and the substrate. Applicants submit that there is nothing in Fisch relating to deflection of the Fisch cover glass.

Tolles refers to the use of "standard thickness glass for which the microscope objectives have been designed, thereby improving the optical quality of images", col. 1, lines 60-62. Fisch recites a preferable range of cover glass thickness of 0.1-0.5 mm as that used for microscopic cell counting with a hemocytometer. There is nothing in Fisch or Tolles that describes, suggests or motivates one to use a cover glass having at least double the preferable thickness, that is, substantially 1 mm.

In addition, the Fisch and Tolles hemocytometers use a thinner cover glass because it passes more light to the specimen on the slide than a thicker cover glass. Therefore, Fisch and Tolles provide no description, suggestion or motivation to use a thicker cover glass and to do so, would impair the use of the Fisch and Tolles hemocytometers.

Application No. 10/021,602  
Amendment dated January 24, 2005  
Reply to Office Action of December 1, 2004

Second, claim 5 requires

a pair of spacer segments attached to the bottom surface of the cover slip, each of the pair of spacer segments extending along substantially a full length of a different one of the opposed edges and forming a hybridization chamber between the spacer segments, the bottom surface of the cover slip and the top surface of the substrate, the hybridization chamber extending substantially to opposite ends of the cover slip

The Office Action at the top of page 3 acknowledges that Fisch does not disclose the claimed spacer segments. In Figs. 1 and 2 of Tolles, the lands 12 are machined in the base plate 11 and are not attached to the cover slip 13 as required by claim 5. The machined lands 12 in Tolles are expensive to create and provide a base plate 11 that is not disposable.

Further, in Tolles, the lands 12 on the base plate 11 do not extend along the edges of the cover glass 13 as required by claim 5. The Office Action, at the top of page 4, argues that there is no stated reason or advantage for placing the spacer segments on the cover glass edges versus having them located on the interior of the cover glass as shown in Tolles. At page 9, line 12, the specification states that "often it is desirable to minimize the width of the ink bars, for example, to about 0.75 mm, so that more area on the cover slip lower surface 56 is available for the chamber 72." Applicants submit that the specification provides motivation to maximize the available area on the cover slip lower surface for the hybridization chamber; and consistent with that objective, the spacer segments are placed along the longitudinal edges of the cover slip. Such a structure is not described nor suggested by Fisch or Tolles.

Applicants submit that a *prima facie* case of obviousness is further not made because the claimed invention is directed to a substantially different problem than Fisch and Tolles. Both Fisch and Tolles are directed to a hemocytometer for precisely counting cells under a microscope within a calibrated grid area. To minimize the counting time and effort, the counting grids are relatively small in area. Further, both Fisch and Tolles show the supporting structure for the cover glass to be inside its peripheral edges, which provides greater support around the counting grid and

Application No. 10/021,602  
Amendment dated January 24, 2005  
Reply to Office Action of December 1, 2004

minimizes deflection over the counting grid. Thus, the combination of Fisch and Tolles does not provide any description, suggestion or motivation to move the supports for the cover glass to the peripheral edges of the cover glass.

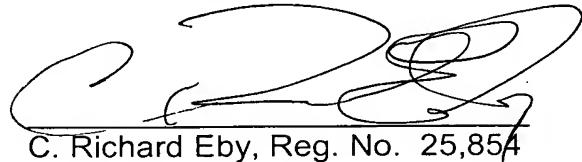
However, in contrast to using a smaller area under the cover glass, Applicants placed the supporting spacers along the cover slip edges to maximize the size of a hybridization chamber. In doing so, Applicants discovered that upon injecting hybridization fluid beneath the cover slip, the fluid adhesion forces are sufficient to deflect the commonly used thinner cover slips. Such deflections vary the distribution of the microarray and hybridization fluid under the cover slip, which can lead to an inaccurate analysis. Applicants further discovered that a cover slip of substantially 1 mm or more in thickness does not deflect and hence, does not adversely affect the hybridization reaction. The combination of Fisch and Tolles does not provide any description, suggestion or motivation to use a cover glass having a thickness of substantially 1 mm, which is sufficient to provide a beam stiffness preventing adhesion forces from changing a distance between the cover slip and the substrate.

Applicants submit that Fisch and Tolles in combination do not express, suggest or motivate one to provide the structure for a hybridization chamber recited in claim 5. Therefore, Applicants submit that the combination of Fisch and Tolles fails to provide a *prima facie* argument of obviousness, and that claims 5 and 43-57 are patentable and not obvious under 35 U.S.C. §103(a) over Fisch in view of Tolles.

Application No. 10/021,602  
Amendment dated January 24, 2005  
Reply to Office Action of December 1, 2004

Applicants respectfully submit that the application is now in condition for allowance and reconsideration of the application is respectfully requested. The Examiner is invited to contact the undersigned in order to resolve any outstanding issues and expedite the allowance of this application.

Respectfully submitted,



C. Richard Eby, Reg. No. 25,854

WOOD, HERRON & EVANS, L.L.P.  
2700 Carew Tower  
Cincinnati, OH 45202  
• (513) 241-2324  
(513) 241-6234 (Facsimile)  
reby@whepatent.com (Email)